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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/889,807	03/01/2002	Michael Almstetter	56268 (41925)	9002

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EXAMINER

KENEDY, ANDREW A

ART UNIT	PAPER NUMBER
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1631

DATE MAILED: 05/28/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/889,807

Applicant(s)

ALMSTETTER ET AL.

Examiner

Andrew A. Kenedy

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-3 and 5-63 is/are pending in the application.
- 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 1-3 is/are rejected.
- 7) ☒ Claim(s) 5-63 is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 20 July 2001 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
- 1) ☒ Certified copies of the priority documents have been received.
 - 2) ☐ Certified copies of the priority documents have been received in Application No. ____.
 - 3) ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. ____. |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date ____. | 6) <input type="checkbox"/> Other: ____. |

DETAILED ACTION

IDS Document No. AA was not considered because the submitted document does not contain sufficient formal identifying information to indicate that it is a reprint/copy of the original, or otherwise.

Claim Objections

Claims 5-63 are objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim *cannot depend from any other multiple dependent claim*. See MPEP § 608.01(n). Accordingly, the claims 5-63 have not been further treated on the merits.

Claim Rejections - 35 USC § 112

Claims 1-3 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claim 1, step (1) requires "selection of M different starting materials suitable for multicomponent reactions (MCRs)". Applicants disclose in the specification that suitable materials for the method are those "provided with functional groups customary in organic chemistry and suitable for multicomponent reactions (MCRs)". Since there are at least millions of such compounds, Applicants provide insufficient guidance to the user regarding making an appropriate selection of starting materials so as to discover a product having the desired properties as in step (8), while still fulfilling the preamble goal of having the method be fast and efficient (e.g., economically practical). In a discussion of the need to decrease the time scale for

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clinical compound discovery using structure-based drug design and combinatorial chemistry methods for lead compound optimization, Nienaber et al. (*Nature Biotechnology*, 2000) explains that "A critical juncture in the process is the identification of a proper lead compound, because a poor choice may generate costly difficulties at later stages" (see pg. 1105, col. 1, paragraph 1). This further supports the Examiner's position that without further guidance or positive active steps in the method, one of ordinary skill in the art would not know how to choose a practical set of starting materials from millions of choices, to subsequently obtain products having all desired properties, where execution of Applicants' method will necessarily produce those products in a manner that is both fast and efficient.

Claim 1, step (6) requires "provision of at least one variant of at least one of the starting materials". This limitation does not provide any criteria for choosing the type of variant to provide. Without additional guidance or positive active steps in the method, one of ordinary skill in the art would not know what variant to provide in order to successfully execute Applicants' method in a fast and efficient manner.

Claim 1, steps (3) and (4) require performing analysis and evaluation of synthesized products, respectively. Since step (1) does not limit the number of different starting materials that can be used in the synthesis reaction of step (2), an unlimited number of materials can theoretically be used. However, Young et al. (*J. Chem. Inf. Comput. Sci.*, 2003) explains that "For a given reaction or sequence of reactions, the number of possible products can be astronomical. For example, Tan et al. executed a multistep reaction starting with 18 tetracyclic scaffolds and combined these with 30 alkynes, 62 primary amines, and 62 carboxylic acids giving a total of 2.18 million distinct final products" (see pg. 1916, col. 1, paragraph 2). Young

et al. states that in general, "with multicomponent reactions, there could easily be millions to billions of possible products" (see the abstract). With millions to billions of products resulting from a multicomponent reaction encompassed by Applicants' method, one of ordinary skill in the art would not know how to perform the full range of analyses and evaluations encompassed by steps (3) and (4) of the method respectively, in a fast and efficient manner, without additional guidance or positive active steps in the method.

Claim 1 reads broadly to encompass not only physical methods of compound discovery and preparation, but also *in silico* methods. However, Applicants disclosure teaches only physical methods of synthesis and *in vivo* testing of compounds. One of ordinary skill in the art would not know how to execute Applicants' method as claimed *in silico*, without additional guidance or positive active steps in the method.

Claims 1-3 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Regarding Claim 1, the preamble indicates that Applicants' method for discovery and preparation of new compounds is "fast and efficient". The terms "fast" and "efficient" are relative terms that are not disclosed by Applicants in quantitative terms. Because the claimed method leaves it up to the discretion of the user to choose the number and type of starting materials in step (1), product(s) in step (4), variant materials in step (6), and desired property/properties in step (8), Applicants' method is not necessarily a fast and efficient method, and in fact, in the hands of certain users making poorly guided choices, may require a very large

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number (or perhaps infinite) number of iterations to reach the requirement of step (8) and find a product having the desired property.

Regarding Claim 1, the preamble goal as stated is "the fast and efficient discovery and preparation of new compounds". Since step (9) is indicated as being optional, step (8) can be considered to be the last required step of the method. Step (8) requires reiterating the method "until at least one product having the desired property or properties is found". This requirement is inconsistent with the preamble goal. In actuality, discovery and preparation of new compounds may occur as early as step (3) during a first iteration of the method as claimed. It is unclear why a user of the method must proceed further than step (3) to achieve the preamble goal. Furthermore, step (8) allows for termination of the method once a product having a desired property is found, without requiring that the product be new (novel and uncharacterized), as required by the preamble goal. Therefore, the method steps are inconsistent and confusing with respect to the preamble goal.

Claim 1, step (3) requires "analysis of the products". This limitation is indefinite as to what the products are being analyzed for, thereby rendering the scope of the claim uncertain.

Claim 1, step (4) requires "evaluation of the products and selection of at least one product". This limitation is indefinite as to what the products are evaluated for, thereby rendering the scope of the claim uncertain. It is also confusing as to whether and how this "evaluation" differs from the "analysis" required in the previous method step. The limitation is also unclear as to the criteria used for selecting products.

Claim 1, step (6) requires "provision of at least one variant of at least one of the starting materials". This limitation is unclear as to what constitutes a variant, thereby rendering the scope of the claim uncertain.

Claim 1, step (7) requires "reaction of the starting materials provided in (6) if appropriate". This limitation is unclear as to the criteria to be used for making a determination of whether performing the reaction would be appropriate.

Claim 1, step (8) requires "repetition of steps (4) to (7) until at least one product having the desired property or properties is found". It is unclear when (at which step in the method) the user picked a desired property and when the products are tested for the desired property, since no previous step in the method requires either of these operations. Furthermore, the immediately preceding step (7) does not require testing products for a desired property/properties.

Claim 1, step (9) requires "optionally isolation and characterisation of the product". The limitation is indefinite as to what type(s) of characterisation of the product is required, thereby rendering the scope of the claim uncertain.

Claim 3 requires "reaction conditions suitable for MCRs are also selected". This limitation is indefinite as to the type of reaction conditions encompassed, thereby rendering the scope of the claim uncertain.

Conclusion

Prior art of record that discloses aspects of Applicants' instant invention but was not relied upon: Kiely et al. (US 5874443 A) teaches the reacting of pairs of compounds in a high throughput grouped format, proceeding sequentially through a series of grouped reactions to eventually

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produce a large and diverse combinatorial library of product compounds. However, Kiely et al. does not teach reacting each material of a group of M different starting materials with every possible combination, from 2 to M-1, of the other starting materials as in Applicants' instant invention.

Contact Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Andrew A. Kenedy whose telephone number is (571)-272-0574. The examiner can normally be reached on Monday-Friday 9:00am-5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward can be reached on (571)-272-0722. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

A.A.K. May 26, 2004

Marianne P. Allen
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PRIMARY EXAMINER
5/26/04
Au1631